The Construction and Validation of a New Ovarian Malignancy Probability Score (OMPS) for Prediction of Ovarian Malignancy

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Abstract

Background: The best management for an ovarian mass is provided by appropriate prediction of malignancy. The aim of our study is to construct and validate a new Malignancy Probability Score based on four simple sonographic findings and age.

Methods: In a cross sectional study; histopathological files of 3303 ovarian mass patients and tertiary hospitals, have reviewed within 6 years (2000-2006). Pathology, age, sonographic findings including solid area, ascetic, size and bilateralism were recorded. Logistic multivariate regression analysis SPSS18 has used to create malignancy probability scoring model. Our ovarian Malignancy Probability Score (OMPS) has constructed based on 80% of samples in a logistic regression model and has validated using the remainder of the cases.

Results: Ovarian malignancy probability score (OMPS) has calculated as follow: age $\times$ 0.062 + Tumor size (cm) $\times$ 0.012+1.172(if the tumor is solid) + 1.289(if ascites is present) +0.758(if the tumor is bilateral)

Sensitivity of OMPS in prediction of malignancy with cutoff value of 3.65 score number was 77.9% and its specificity was 72.9% with Area under Curve (AUC) of 83% in ROC curve.

Conclusion: OMPS is designed and tested in our research, to be proved as a simple and accurate clinical tool for ovarian malignancy prediction.

Key words: Logistic model; Ovarian mass; Ovarian cancer; Ultrasound; Risk of malignancy

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Introduction

Ovarian cancer is a common malignancy; among the females in different populations would be 4th 7th most frequent ones [1-7].

Ovarian cancer is the leading cause of death due to a gynecologic malignancy [1, 8-12]. Therefore it is a matter of public health [1, 4].

In Iran, ovarian cancer is the 8th most frequent cancer and the 12th cause of death and the 16th in burden of malignancy among women [13].

Survival of ovarian cancer has been reported in the 25% to 61% of different reports from Asian countries, western countries and Australia [1, 4, 14-20].

In malignant ovarian masses, optimal surgical debulking and appropriate staging, both Play the most important roles in improving survival [21-22].

In Most cases of advanced ovarian cancers, they have been operated in primary care hospitals, caused worse results in both prognosis, and higher mortality and morbidity [23-24].The best prognosis of ovarian cancer has achieved when gyneco-oncologists manage the patients [25].

In the management of an adnexal mass, prediction of the chance of malignancy enables the surgeon to select proper surgical route (laparoscopy or laparatomy) and surgical incision (midline or transverse) and appropriate referral to expert

gyneco-oncologist surgeons who mostly work in tertiary care hospitals [26].

There are many different functional parameters to predict risk of malignancy in an ovarian mass including morphologic characteristics of the mass as observed in sonography, serum CA 125, Doppler velocimetry, menopausal status and age.

Several predicting methods have been constructed; using different combinations of above mentioned factors like Sassoon's Model, Risk of Malignancy Index (RMI) number 1-5; and Artificial Neural Network [27-44].

Sonographic features are considered valuable to predict ovarian malignancy [45-48]; with acceptable sensitivity and specificity [49].

In the present study; age plus four simple sonographic findings; are used in construction of a new method of prediction called "Ovarian Malignancy Probability Score" (OMPS).

We have selected these factors because of their simplicity and availability in all settings; including primary, secondary and tertiary care hospitals. We suggest OMPS as a guide for clinicians to improve management of ovarian masses.

Materials and Methods

In a cross sectional analytical study, histopathologic files of ovarian masses which selected from 20 pathology departments of 20 tertiary and secondary care hospitals in Tehran (17 centers) and Hamadan (3 centers); have reviewed from 2000 to 2006 . Cases which have operated on due to causes other than ovarian mass such as abnormal bleeding, myoma or other indications have excluded.

The ovarian masses, till 3 centimeters in size before surgery, have excluded either. Finally 3303 surgeries on ovarian masses have included in our study and age plus 4 sonographic findings including size, solid area, ascites and bilateralism have recorded.

Age has documented based on the information recorded in patient's files and sonographic findings have recorded according to written report of abdominal sonography.

For describing data, we utilized mean, standard deviation, median, 95%CI, frequency and percentage.

Randomly about 20% of samples have set aside for later validation and remained 80% included in a logistic regression model to derive weight of each factor in ovarian malignancy probability score. In order to find the best cutoff value; we utilized some criteria such as sensitivity, specificity, likelihood ratio and youden Index.

Finally, the accuracy of the model has validated on 20% of sample population who were not included in model construction. All statistical analysis has performed using SPSS version18.

Results

Malignant pathologic results have found in 175 out of 3303 (5.4%). Mean ±SD of the study population has 35±0.2 (median: 33, range: 9- 83). Mean and median diameter size of the tumors were 6.9 (±0.7) and 6 (3-50) centimeters, respectively.

Sonography have found solid area in 382 (11.7%), asceites in 531 (16.3%) and bilateralism in 308 (9.4%) of the cases .Table 1 demonstrates the characteristics of participants by the malignancy existence.

All of the factors including age, tumor size, solid area, aseites and bilateralism were high relevant to malignancy in univariate analysis (Table 1).

Two thousand and five hundred and fifty selected samples randomly have included in multivariate analysis and logistic model construction, then and the other cases have utilized in model validation .Weight of each five factors that have been used in logistic regression analysis, are shown in table 2.

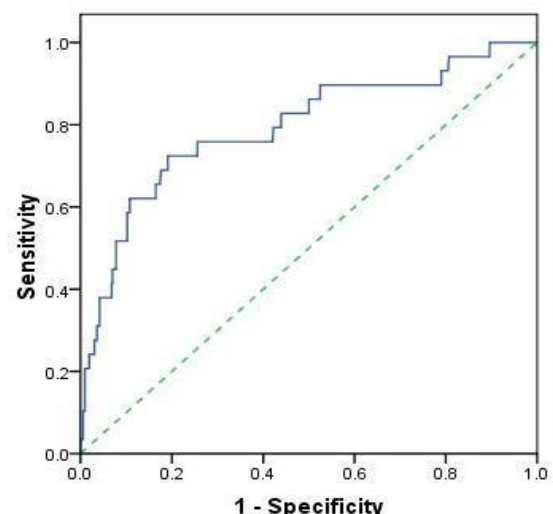As a result, Malignancy Probability Score (OMPS) formula has determined as follow:

OMPS=Age×0.062 + Tumor size (cm) × 0.012+1.172(if the tumor is solid) + 1.289 (if ascites is present) +0.758(if the tumor is solid)

Figure 1. ROC curve of OMPS in scores above 3.65 as cutoff value for malignancy prediction (AUC = 83% 95% CI: 79-87%)

In our research, for finding the best cutoff value, we have considered likelihood ratio and youden index. Score number of 3.65(malignancy probability =5%, and likelihood ratio= 2.41) has selected as cutoff value of malignancy prediction, 77.9%sensitivity, and 72.9% specificity (Fig 1).

Validation of the model has done by the 480 (20%) of total cases, whom have not included in model production. In this statistical model (OMPS), subjects has recalculated with cutoff value of 5% prediction of malignancy, 77.6% sensitivity, and 72.5%specificity (Fig1).

Discussion

The key point for appropriate ovarian mass management is prediction of malignancy.

Morphologic sonographic findings, Doppler sonography, color Doppler flow imaging and combined methods are among important parameters.

In a Meta-analysis, among 5159 cases, 46 studies have compared together [50]. ROC curve of combined methods, have revealed Q point (intersection between curve and diagonal in equality of sensitivity and specificity), much higher than the Q point of methods using only sonographic features (p=0.003), or Doppler sonography alone (p=0.003) and Color Doppler Flow Imaging alone (p=0.001) [50-52].

In these Meta-analyses; sonographic features were alone superior if compared to Doppler Sonography alone, or color Doppler flow imaging alone in prediction of ovarian mass malignancy [50].

In a comparative study, malignancy predictive value of serum CA125, sonographic features and Risk of Malignancy Index or RMI (A method of prediction based on menopausal status, sonography and serum CA125) have compared.

All three above mentioned methods were relevant malignancy predictors but the combination method (RMI), have obtained the best predictive performance [46].

Sonography alone is highly sensitive in detection of ovarian masses, but its specifity is comparatively low [28, 53-54].

Many study results confirm that sonography is a valuable discriminator between benign and malignant ovarian tumors [47, 48, 50, 55-56].

If sonographic findings have combined with other parameters such as age, serum CA-125 level, doppler and color doppler findings, the accuracy of malignancy prediction would be increased [56-58].

Doppler and color Doppler imaging require more experience, but time consuming, and not available in all settings [51, 52].

serum CA 125 is not expensive and seems to be a valuable factor in a clinical scoring system .We have

Table 1. Comparison of age plus 4 sonographic findings in malignant and benign cases

Factor	Benign n = 3123	Malignant n = 179	Diff (95%CI)	P-Value
Mean age± SD, yrs	35 ± 12	45 ± 16	10(7.6-12.4)	<0.001
Mean size ± SD, cm	10 ± 5.2	6.7 ± 3.7	3.3(2.7-3.9)	<0.001
Solid area n (%)	325 (10)	62 (35)	24(17-31)	<0.001
Ascites n (%)	478 (15)	59 (33)	18(12-15)	<0.001
Bilateralism n(%)	274 (9)	38 (21)	13(7-19)	<0.001

Table 2. Regression sums of ovarian malignancy probability score for each parameter in study population

Factor	Regression sum	SE	Significance	AOR[1] = expel (rs)[2]	95%CI (AOR[1])
Age	0.062	0.007	0.000	1.064	1.051-1.078
Size (cm)	0.012	0.002	0.000	1.012	1.008 – 1.015
Solid area	1.172	0.227	0.000	3.230	2.070 – 5.039
Ascites Bilateral	1.289	0.216	0.000	3.628	2.377 – 5.536
	0.758	0.256	0.003	2.135	1.293 -3.523

1. AOR: Adjusted Odd's Ratio

2. expel (rs): Exponential of Logistic regression coefficient

reviewed the documents of our study population regarding the preoperative assessment before ovarian tumor operations .

In all of them, sonography has done at least once. Serum CA-125 testing has done in only 301(9.7%) out of 3303 and Doppler imaging results have found in just 50 (1.5%). [59].Many factors have contributed in, because some Gynecologists have ordered serum CA125 before ovarian tumor surgery. They might not be aware of the predictive value of the test, or be in a hurry to operate on in order to shorten the hospital stay, or preoperative waiting time of their patients.

The cost of the serum CA-125 test and/ or the long time to receive the test result in some areas, especially local hospitals, might also play a role.

Considering the different sonographic findings to predict malignancy, a Neural Network model has found the tumor size and the existence of solid areas in tumor as the most relevant factors to malignancy [55].

Another study has found papillary projections of the tumor wall and solid areas as the only sonographic independent predictors of malignancy [58].

A study based on multivariate analysis, have shown solid areas and bilateralism of ovarian mass, as the only independent predictors of malignancy [46]. Risk of Malignancy Index (RMI) , as mentioned to be the most relevant method to malignancy [46] has first used by Jacobs et al.It is based on 5 sonographic features (multilocular cyst , solid area , ascites , bilateralism and evidence of metastasis)menopausal status and serum CA125 level. Positive finding of each sonographic factor is scored one where negative finding gets zero. If more than one positive finding is present in the patients, then its sonography gets score3.If the case is postmenopausal, it gets 3 and if she is premenopausal the score is 1 for menopausal status.

RMI is the product of: sonographic score $\times$ menopausal score $\times$ CA -125 levels; and is considered the method of choice to predict risk of malignancy in multiple validation studies [27, 28, 33, 46, 58].

RMI using cutoff value of 200; achieves 70-87% sensitivity and79% specificity. Ninety seven percent OMPS with cutoff value of 3.65 shows sensitivity of 77.6% and specificity of 72%. Five percent with AUC of 83% in ROC curve (Fig 1), which is comparable with RMI specially considering the sensitivity .In RMI if sonographic features would be in favor of benign mass and its score would be zero, then the risk of malignancy drops to zero.

So, the impact of two other parameters including menopausal status and serum CA-125 (each one a malignancy relevant predictive factor) are neutralized. In the other hand, effect of tumor size even in a simple and benign appearing mass is not considered in RMI.For instance a 15 cm simple cyst with a serum CA-125 level of 500 in this method shows no risk of malignancy which would need some modifications.

Other notable point in RMI is ignoring the age and considering the menopausal status as the only age related factor. In this way it puts a 50 and 70 years old patient at the same risk level while two 48 years old patients who are pre and post menopausal will be scored differently.

Based on these observations we have selected age plus 4 simple sonographic findings which are accessible in all setting including tertiary, secondary and primary – local hospitals, to provide an ovarian malignancy probability score (OMPS).

In the present study, weight of age (each years of life) and size of tumor (each centimeter) are considered in logistic regression analysis. Qualitative conditions such as solid area, ascites and bilateralism, the weight of each parameter in logistic regression is considered more carefully. Less specificity of our study method, OMPS, although acceptable (72. 5%), compared to RMI (79-97%) might be due to exclusion of serum CA 125 in OMPS method.

Some limitations of the present study should be considered, sonographists have been in different levels of experience, although all of them were radiologists at least in level *II* experience and none of the reports have provided by assistants in training. Although the study was multicentre and wide ranged, study population have operated in Tehran city (17 hospital) and 3 hospitals of Hamadan province. Population Malignancy frequency has been estimated 5.4% which is nearly equal to overall risk of malignancy in ovarian masses. In this regard, the study population seems to be representative of general population of women.

Ovarian malignancy probability score (OMPS) is suggested for prediction of ovarian mass malignancy with acceptable sensitivity and specificity based on very simple and relevant sonographic parameters plus age.

Clinicians would be guided by OMPS regarding route of surgery (laparoscopy or laparatomy) and referral to tertiary hospitals with surgeons more specialized in cancer surgery in the case of high score which results in better management and survival of ovarian cancer patients.

Acknowledgements

Conflict of Interest

Authors' Contribution

MA has designed the study, participated in data collection and analysis and wrote the paper. MY have analyzed the data, supervised data entry and revised statistics of the paper. MF,AM and AT have participated in writing the paper.KSH has revised and edited the paper.

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